**Improper function of ER – leads to wrong protein folding/export**

Hyperthyroidism

Osteogenesis imperfecta (defective collagen production)

Cystic fibrosis –Cl channels are mutated (usually deltaF508CFTR) and usually do not reach the surface. Accumulation of Cl in cells causes increased Na to enter cells, and water follows. Leads to dry mucus.

**Mitochondria**

Cardioencephalomyopathy

Deafness

Type II diabetes

**Peroxizomes** – Zellweger’s syndrome

**Respiratory** acidosis: acidic blood because of hypoventilation (buildup of CO2), due to head (tumors, drugs)/lung problems

Respiratory alkalosis: basic blood because of hyperventilation (lack of CO2), due to anxiety, drugs, lung disease, fever/stroke

H + HCO3 -> H2CO3 -> H2O + CO2

**Prions –** disease caused by beta-sheet prions that are insoluble (normal are alpha helices and soluble)

Transmissible spongiform encephalopathies (TSEs)

In humans, Creutzfeld-Jakob disease (CJD)

* Sporadic (idiopathic), inherited, iatrogenic, and variant (caused by BSE)

Only transmissible in mice with regular prions already

**Hyperkeratinosis** – compromised tissue structure (mutations in skin)

**Nuclear lamina** – mutation of Lamin A gene leads to progeria

**Cancer** – often abnormal number of centrosomes. Characterized by unrestrained cell division and invasion of outside territories

HPV gene product E6 sequesters p53 and E7 sequesters Rb, often causing cervical cancer

Loss of both RB alleles causes retinoblastoma. 40% heritable, 60% sporadic. Cone cells susceptible because they express high levels of MDM2

Amplified cyclins and CDK expression in many tumors. Also CDKI mutations such as p16 (normally causes senescence in response to too much division or damage). P16 mutation is the largest known genetic cause of melanoma

P53 is most commonly mutated gene in cancer

**Spectrin and ankyrin**– Hereditary Spherocytosis caused by defects in spectrins and ankyrin – altered cytoskeletal architecture; leads to anemia and splenomegaly (too many RBCs). HS cells are bad at gas exchange and squeezing through junctions. Autosomal dominant.

**T-helper cells** – HIV targets CD4 recepter and CCR5 coreceptor; when cell count <200/mm2, AIDS

**Membrane proteins**

Cancer -alterations of membrane is key to metastasis

Diabetes – defective insulin signaling and function of glucose transporters

Heart disease (arrhythmias) – defective cell-cell communication

Primary **ciliary** diskynesia (Kartagener’s syndrome) – lack dynein cross-arms or radial spokes. Immotile cilia leads to lung infections, mucus buildup, infertility, heart malrotation

**Macula Adherens (desmosome)** – phemphigus vulgaris is an autoimmune disease with antibodies to desmoglein (a cadherin). Severe blistering from water-loss, infections are life-threatening

**Scurvy –** vitamin C is a cofactor for prolyl hydroxylase (P residues are normally hydroxylated in collagen protein)

**Nicotinic Acetylcholine receptor** – myasthenia gravis is an autoimmune disease; antibodies target the nACHR’s . muscle weakness, especially in face. Treatments = acetylcholinesterase inhibitors, immunosuppresives

Week 2:

**Hemoglobin** – betaGlu6->Val mutation leads to Hemoglobin S, aka sickle cell anemia. Disease=homozygous; hetero=asymptomatic

-Hemoglobin C disease, betaGlu6->Lys, has less severe anemia, leads to HbC.

Order of decreasing severity (genotype): S/S > S/C > C/C > everything else is asymptomatic

-both diseases confer malarial resistance

-in sickle cell, mutation causes aggregation of Hb molecules, preventing O2 binding.

-thalasemmias result from deletions of genes from alpha or beta chain (beta thalassemmias can also be caused by other errors in protein formation)

**Integrin­ –** improper integrin leads to Leukocyte Adhesion Deficiency; leukocytes cannot properly adhere to blood vessel and therefore cannot extravasate. Leads to life-threatening infections

* Lack of beta3 integrin causes excessive bleeding because of lack of clotting. Glanzmann’s disease

**Adipocytes** – hypercellular (hyperplastic) obesity results from too many white adipocytes. Caused by overfeeding as an infant. This is more serious than hypertrophic obesity, which is caused by increased size of cells

**Mast cells/inflammatory cells** – too much release of granular substances like histamine leads to anaphylactic shock. Blood fluid diffuses into EC matrix.

**Collagen**

Ehlers-Danlos Type VII – non-functioning procollagen peptidase leads to hyperflexible joints, dislocations, and soft skin

Ehlers-Danlos Type IV – deficiency in collagen type III leads to aneurysms and intestinal rupture and weak blood vessels

**Elastin**

Emphysema – breakdown of lung elastic fibers

Marfan’s syndrome – poor microfibril formation. Blood vessels rupture, aneurysms

**Interstitial fluid** – “pitting edema” can be caused by blocked lymphatics, block veins, liver disease, increased vascular permeability, hypertension, and starvation

-myxedema is caused by overproduction of GAGs in hypothyroidism